



UNITED STATES PATENT AND TRADEMARK OFFICE

c/v

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,825	02/19/2002	Wolfgang M. Franz	0690-0115P	6306
2292	7590	06/20/2005	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			LI, QIAN JANICE	
			ART UNIT	PAPER NUMBER

1632

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/049,825	Applicant(s) FRANZ, WOLFGANG M.	
	Examiner Q. Janice Li, M.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-59 is/are pending in the application.
- 4a) Of the above claim(s) 47-49 and 53-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-46, 50-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response and amendment filed 4/19/05 have been entered. Claims 34, 36, 37, 46 have been amended. Claims 53-59 are newly submitted.

Newly submitted claims 53-59 significantly broadened the scope of the invention as originally claimed for the following reasons: the new claims are drawn to a genus of expression cassettes that contain (i) a polynucleotide comprising a cardiac tissue-specific promoter operatively linked to (ii) a polynucleotide encoding extracellular and transmembrane domains of receptor expressed by a B or a T cell; whereas previously presented claim 34 embraces expression cassettes comprising elements (i) and (ii), and additionally at least one IRES operably linked to at least one polynucleotide encoding an angiogenesis factor. Although the new claims embrace the various expression cassettes presented previously, they further encompass an enormous amount of expression cassettes having different combination of elements (promoters, enhancers, transgenes, having/lacking IRES elements, etc.). It is noted claim 34 already encompasses at least 7 different subgenus/species of expression cassettes varied in the type of expression control elements and transgenes expressed. The newly presented claim 53 further greatly extended the genus that encompasses the numerous species of expression cassettes.

37 CFR § 1.141 instructs when more than one species of invention are claimed in a national stage application, the species should not to exceed a reasonable number. Since the applicant has received more than one action on the merits for the previously

Art Unit: 1632

presented invention, since a reasonable numbers of species have been examined in this application, this invention has been constructively elected by original presentation for prosecution on the merits. If not to restrict, the expression cassettes encompassed by the claimed genus are uncountable, and thus exceeded a reasonable number.

Accordingly, claims 53-59 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 34-59 are pending in the application, claims 47-49, 53-59 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 34-46, 50-52 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and arguments will not be reiterated. The arguments in 4/19/05 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-46 and 50-52 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1632

The amended claims recite, "a constitutive enhancer". The specification fails to define what enhancer it encompasses or excludes, and thus the metes and bounds of the claims are uncertain.

The amended claims recite, "a promoter operative in a mammalian ES cell, primordial cell or bone marrow stromal cell". The specification fails to define what type of promoters are encompassed or excluded by the phrase, and thus the metes and bounds of the claims are uncertain. Since many strong promoters, such as a CMV promoter, a SV40 promoter would operate in an ES cell, the phrase appears to encompass many promoters, not limited to ES cell-specific promoter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-46, and 50-52 stand and newly rejected under 35U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed for reasons of record and following. The original disclosure fails to specify a genus of constitutive enhancers, or a genus of promoters operative in a mammalian ES cell, primordial cell or bone marrow stromal cell".

The specification as originally filed discloses a PGK promoter and a CMV enhancer, and is completely silent with respect to the genus of promoters operative in a mammalian ES cell, primordial cell or bone marrow stromal cell; the specification fails to teach the association of the PGK promoter with the genus as now claimed, and

Art Unit: 1632

representative promoters that belong to this genus. Thus, the amendment is a departure from and an addition to the disclosure of the application as filed; accordingly, it introduces new matter into the disclosure. Likewise, the specification is completely silent with respect to the genus of constitutive enhancers, the association of the CMV enhancer with the genus as now claimed, and thus the amendment is a departure from and an addition to the disclosure of the application as filed; accordingly, it introduces new matter into the disclosure.

MPEP 2163.02 teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION".

In the response of 4/19/05, applicants improperly characterized the issue under this rejection as "lack of written description". Here, applicants are reminded this is a new matter rejection, not an ordinary test for sufficiency of written description. The application as filed describes a single PGK promoter, but there is no teaching or even contemplation of the genus of the promoters as now claimed, thus, the amendment departs from and adds to the original disclosure, even though the PGK promoter may have a property of "operative in a mammalian ES cell, primordial cell or bone marrow stromal cell", and even though at the time there might be other promoters known to meet the limitation. Likewise, the application as filed describes a single CMV promoter,

Art Unit: 1632

but there is no teaching or even contemplation of the genus of “constitutive enhancers”, thus the amendment departs from and adds to the original disclosure even though the CMV enhancer does have a property of constitutive expression in mammalian cells. Here, what was known in the art cannot substitute what was disclosed in the application as filed.

Additionally, the amended claims recite, “a promoter *operative* in a mammalian ES cell...”. This amendment appears to have changed the claimed expression cassettes from containing an ES cell-specific promoter to any promoter that function in an ES cell. Thus, when using such cassette in the method of claim 50, the transgene driven by such promoter might continue to express after ES cells are differentiated into cardiomyocytes since the promoter may not be ES cell-specific, and thus the amendment has changed the nature of the invention as filed, and introduced another new matter to the disclosure.

In 4/19/05 response, applicants argued it is not necessary that the exact words of the claims be present in the specification, the showing is one from the specification as a whole.

In response, applicants fail to specifically point out where in the specification, it teaches the concept as a whole of “constitutive enhancer” and “promoter operative in a mammalian ES cell, primordial cell or bone marrow stromal cell”. The specification as filed states “*Therefore the object of this invention is to make available improved means and processes for acquisition of differentiated somatic cells. In particular, the object was to make available improved means and processes for acquisition of differentiated*

Art Unit: 1632

ventricular cardiomyocytes" (Page 5). The specification as filed contemplates the organ-specific or tissue-specific promoter as a whole, but never the "constitutive enhancer" or "a promoter operative in a mammalian ES cell" as a whole. In fact, it is not clear what the new claim recitations encompass or exclude, and thus the specification as filed fails to teach the asserted concept as a whole.

The Remarks of 4/19/05 went on to reiterate previous argument. In response, relevant portion in pages 4-6 of the Office action mailed 10/20/04 are reiterated to address the reiterated argument.

For reasons set forth above, the amendments filed 6/18/04 and 4/19/05 are objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 34-46 and 50-52 stand rejected and newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been adequately described, and that is not conventional in the art.

Art Unit: 1632

Applicants submitted several prior art publications to show that CMV enhancer and Oct-3/4 promoter operative in ES cells are known in the art before the instant priority date. However, as indicated *supra*, since the application as filed is completely silent concerning the genus, what is known in the art cannot substitute what is disclosed in the specification as filed. Moreover, the specification fails to teach how to use the art known Oct-3/4 promoter or any other enhancer in the instantly claimed invention, and thus fails to support the full scope of the claims. The Federal Circuit has stated that:

a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. **It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement.** Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1005 (CAFC 1997) (emphasis added).

The arguments drawn to organ-specific/tissue-specific promoter and selectable markers are moot because they are not the subject matter rejected under this provision.

Accordingly, for reasons of record and set forth *supra*, the instant disclosure fails to satisfy the statutory enablement requirement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 34 (A, B), 35, 38, 39, 40, 42, 46, and 50-52 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Klug et al* (J Clin Invest 1996;98:216-24), *Gaines et al* (IDS, Biotechniques 1999;26:683-8), *Griscelli et al* (Hum Gene Ther 1998;9:1919-28), and *Wolfgang-M et al* (J Mol Cell Cardiol 1997;29(5):A125), and in view of *Mack et al* (J Thorac Cardiovasc Surg 1998;115:168-76), for reasons of record and following.

In the Remarks, Applicants first argued the Examiner fails to establish why one would find it desirable to express a therapeutic gene encoding an angiogenesis factor simultaneously with a marker used for selection of differentiating cells.

In response, such motivation could be found in the combined teachings of *Klug et al* and *Mack et al*. *Klug et al* teach obtaining a relatively pure population of cardiomyocytes for transplantation to repair damaged heart tissue; and *Mack et al* teach supplying angiogenesis factor in addition to other cardiac surgical procedures for enhancing collateral vessel formation and regional perfusion, and improving function of damaged heart tissue. Since the two different modalities serve the same purpose of regenerating damaged heart function, it would have been desirable to combine the two approaches for the common goal of repairing damaged heart function. The court has

Art Unit: 1632

determined that finding obviousness does not require expressly written motivation to combine prior art since the motivation to combine may be found in the nature of the problem to be solved. "FINDING OF OBVIOUSNESS DOES NOT REQUIRE EXISTENCE OF EXPRESS, WRITTEN MOTIVATION TO COMBINE IN PRIOR ART, SINCE MOTIVATION TO COMBINE MAY BE FOUND IN NATURE OF PROBLEM TO BE SOLVED, LEADING INVENTORS TO LOOK TO REFERENCES RELATING TO POSSIBLE SOLUTIONS TO THAT PROBLEM". (*Ruiz v. A.B. Chance Co.*, 69 USPQ2d 1686 CA FC 2004). Here, both *Klug et al* and *Mack et al* teach solving a problem in treating heart disease. Thus it would have suggested to the skilled artisan to look to references relating to possible solutions, and combining such as necessary.

Applicants then argued the Examiner has not explained why the artisan would specifically combine a polynucleotide encoding a receptor expressed on the surface of a B/T-cell with a cardiac tissue-specific promoter.

In response, combining a cardiac tissue-specific promoter with a marker gene has been practiced by *Klug et al*, who teach using a cardiac tissue-specific promoter operably linked to a marker gene so that only cells differentiated into cardiomyocytes could be selected. As to using a lymphocyte surface marker, the answer could be found in the teaching of *Gaines et al*. *Gaines et al* teach a lymphocyte surface marker is suitable for selecting transfected cells via MACS- or FACS-based cell sorting procedure, which marker happens to be a B/T-cell marker, i.e. a nucleic acid encoding the extracellular and transmembrane domain of the human CD4 receptor. Given the numerous marker genes known in the art, given flow cytometry being the most popular means for selecting/sorting living cells, the ordinary skilled would have been motivated

Art Unit: 1632

to use the CD4 marker in the method as taught by *Klug et al* for selecting/sorting the cardiomyocytes. As to the specific combination, the court has decided, "FINDING OF MOTIVATION TO COMBINE PRIOR ART REFERENCES NEED NOT BE SUPPORTED BY SHOWING THAT CLAIMED COMBINATION IS PREFERRED OVER OTHER ALTERNATIVES, SINCE PROPER INQUIRY IS WHETHER THERE IS SOMETHING IN PRIOR ART AS WHOLE TO SUGGEST DESIRABILITY, AND THUS OBVIOUSNESS, OF MAKING COMBINATION, NOT WHETHER THERE IS SOMETHING IN PRIOR ART AS WHOLE TO SUGGEST THAT COMBINATION IS PREFERRED OR MOST DESIRABLE. (*In re Fulton*, 73 USPQ2d 1141 CA FC 2004).

Applicants also argued there is no motivation to make the claimed expression cassettes with the specific promoter-transgene arrangement given the teaching of *Gaines et al*.

In response, in view the levels of the skilled in the art as illustrated by the combined teachings, these limitations fall within the bound of optimization.

Applicants went on to argue that the claimed invention provides results unexpected by one of ordinary skilled in the art at the time the invention was made in terms of the electrophysiology of the selected cells and high purity of the population obtained, pointing to table 1 of *Klug et al*, and submitted exhibit 9 as evidence.

In response, it is noted by *Klug et al* was published in a peer-reviewed, reputable journal, and table 1 of *Klug et al* clearly indicated that using the transfection method (G418 selection), 99.6% cells in the selected cell population are cardiomyocytes, and thus would have the inherent electrophysiological property of a cardiomyocyte. If applicants dispute the fact, it is applicants' duty to prove that these cardiomyocytes do not possess the intrinsic "electrophysiological properties similar to those of a ventricular

Art Unit: 1632

cardiomyocyte" (see instant claim 50). This is because the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the prior art products do not necessarily or inherently possess characteristics of the claimed product, which requires factual evidence demonstrating that actual, unobvious differences exist or that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPBI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922, 1923 (BPAI 1989). Moreover, the rejection was based on the combined teachings; thus, the product of the combined teachings would possess the claimed electrophysiological properties.

As to the exhibit 9, the reviewer generally questioned whether the claimed method as a whole could generate cardiomyocytes. Since the declared cardiomyocytes by *Klug et al* was published in a peer-reviewed, reputable journal, in the absence of evidence to the contrary, the cells are assumed to be cardiomyocytes with the appropriate electrophysiological properties of a ventricular cardiomyocyte.

Additionally, applicants are reminded the unexpected results should be commensurate with the scope of the disclosure. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN

Art Unit: 1632

OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). In the instant case, the disclosure only support using an expression cassette with a CMV enhancer, and a PGK promoter, whereas the currently claimed expression cassettes are drawn to any "constitutive enhancer" and any "promoter operative in a mammalian ES cell, primordial cell or bone marrow stromal cell". Accordingly, the asserted "unexpected results", even if proven true, do not apply to the broadly claimed cassettes.

Claims 34 (C-E), 36, 37, 41, 43-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Klug et al* (J Clin Invest 1996;98:216-24), *Gaines et al* (IDS, Biotechniques 1999;26:683-8), *Griscelli et al* (Hum Gene Ther 1998;9:1919-28), *Wolfgang-M et al* (J Mol Cell Cardiol 1997;29(5):A125), and *Mack et al* (J Thorac Cardiovasc Surg 1998;115:168-76) as applied to Claims 34 (A, B), 35, 38, 39, 40, 42, 46, and 50-52 above, and further in view of *Graham et al* (US 6,080,569), *Gainer et al* (Transplant 1998;66:194-9), and *Lallemand et al* (Transgenic Res 1998;7:105-12), for reasons of record and set forth in the immediate preceding rejection.

Request for Rejoinder

Applicants requested the Examiner to reconsider the withdrawn of claims 47-49 on the ground that the claimed cells comprise the cassette having all of the elements recited in one of the claims presently under consideration.

In response, it is noted the rejoinder practice applies when the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. This is not the case in the instant application, wherein the elected group contains both product and a method of using the product, and the Examiner did not require restriction between product and process claims as previously presented. Thus, the rejoinder practice does not apply to the instant situation.

Moreover, just because the broadly claimed cells “comprise the cassette having all of the elements recited in one of the claims presently under consideration”, the cells do not automatically become allowable, because they must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112.

Accordingly, for reasons of record and set forth *supra*, the restriction stands.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

Art Unit: 1632

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

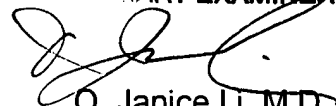
Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
PRIMARY EXAMINER



Q. Janice Li, M.D.
Primary Examiner
Art Unit 1632

QJL
June 10, 2005